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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,822	10/16/2003	Manisha Sharadchandra Deshpande	RELIA.P-113	8483

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 09/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/686,822	DESHPANDE ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,2,5,15,17-21, 24-35* is/are pending in the application.

4a) Of the above claim(s) *1,2,5,15 and 17-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *24-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 2, 5, 15 and 17-21 were withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions. Applicant timely traversed the restriction requirement in the reply filed on 1/23/2006.

Claims 3, 4, 6-14, 16, 22 and 23 were canceled.

New claims 24-35 (7/17/2006) are under examination in the instant office action.

Claim Rejections - 35 USC § 112

New matter

New claims 24-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Insertion of the limitation "at least 3 mm in diameter" in claim 24 has no support in the as-filed specification. The insertion of this limitation is a new concept because it neither has literal support in the as-filed specification by way of a generic disclosure, nor are there specific examples of the newly limited species that would show possession of the concept of the whole ranges from "at least 3 mm in diameter" and more for a construct of tissue-like organization of cells free of scaffold or matrix.

The as-filed specification is lacking description of a cellular mass having diameter of 3 mm as required by the instant claim 24. The as-filed specification only describes a diameter of a culture vessel for growing cells (page 16, par. 1) not a diameter of isolated cell mass. The

diameter of the culture dish for growing cells is 3.5 cm (page 17) or from 0.75 cm to 8,5 cm (page 10). The "tissue-like organization of cells" is inside the culture dish (figure 1). Yet, the claimed invention is drawn to a construct of tissue-like organization of cells that is free of scaffold or matrix. Thus, although the diameter of the culture vessel might affect the final volume of collected cell mass, the disclosed concept of a dish diameter is unrelated to the claimed concept of a tissue-like organization of cells that is free of scaffold as required by the claimed invention.

In alternative, given a broadest interpretation of the claimed concept and as based on the figure 1 showing, the tissue-like organization of dermal fibroblasts is still more than the claimed size "at least 3 mm in diameter".

This is a matter of written description, not a question of what one of skill in the art would or would not have known. The material within the four corners of the as-filed specification must lead to the generic concept. If it does not, the material is new matter. Declarations and new references cannot demonstrate the possession of a concept after the fact. Thus, the insertion of limitation "at least 3 mm in diameter" is considered to be the insertion of new matter for the above reasons.

Indefinite

New claims 24-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 is indefinite because it is unclear what are components of the claimed product and what are the final properties of the claimed "tissue-like organizations of cells". The specific

definitions are lacking in the specifications and the "tissue-like organizations of cells" are broadly described by applicants as "living, cellular, tissue substitutes" (page 13, last par.). The presently claimed product appears to be presented in a form of a product-by-process. However, manipulation steps are not clearly pointed out. For example: in claim 24 it is unclear whether "a culture vessel" remains as a component of the claimed product. In the light of specification the claimed diameter is intended for a culture vessel not for a tissue-like organization of cells. Further, the claimed phrase "free of the requirement of a scaffold or a matrix" also renders the claimed invention indefinite because even if the claimed cells are grown in the absence of matrix, the final product does not exclude matrix or scaffold as claimed. The culture vessel of claim 24 is a 3D-scaffold in a broadest sense. Claims 33 and 34 recite the use of a matrix that is excluded by claim 24. Thus, the metes and bounds of the claims cannot be determined.

With respect to the claims 26 and 30 it is uncertain what components are included in the final product and what components are excluded from the final product. For example: claim 30 recites that cells are grown in a serum containing medium but claim 26 excludes "chemicals" and "growth factors" that are within the serum.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

New claims 24-35 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,755,814 (Berg et al.).

Claims are directed to a 3-dimensional cell mass or a 3-dimensional tissue-like preparation of cells with a diameter of at least 3 mm and more, wherein the cells have been grown in the absence of matrix and wherein the cells are dermal fibroblasts. Some claims are further drawn to the use of cells that have been grown in a basic serum supplemented medium, at initial cell density of $3x10^5$ cells/cm^2 and in some basic culture vessel.

US 5,755,814 (Berg et al.) discloses a preparation of dermal fibroblasts grown in a simple culture vessel using a basic DMEM supplemented with serum and in the absence matrices (col. 9, lines 38-46). The cited patent teaches that fibroblasts attached to plastic dishes and proliferated better without matrices than fibroblasts in the presence of matrices. The cultured dermal fibroblast preparation grown as a sheet-like uniform layer of cells on plastic surface of the culture dish without matrices is considered to be the same cell preparation as the presently claimed "tissue-like organization of cells" within the meaning of the claims and in the light of specification. The fibroblasts are seeded at starting density of $3x10^5$ cells per a well having at least 0.9 cm diameter (col. 9, line 41) and thus, the final cell mass has a diameter of at least 3 mm and more within the meaning of the claims. Considering the disclosed diameter of 0.9 cm (col. 9, line 41) the cells density per cm^2 would be about 4.8×10^5 cells/cm^2 [3×10^5 cells/0.63 $cm^2 = 4.8 \times 10^5$ cells/cm^2, wherein $\pi r^2 = 3.14x(0.9cm/2)^2 = 0.63$ cm^2]. US 5,755,814 also teaches preparation of dermal fibroblasts with a matrix as encompassed by claims 33 and 34 that is made with the same cell density $3x10^5$ cells per a well or 4.8×10^5 cells/cm^2 of a matrix.

Therefore, the cited patent US 5,755,814 (Berg et al.) anticipates the claimed invention.

Claims 24, 25 and 27-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Furukawa et al. ("Formation of human fibroblast aggregates (spheroids) by rotational culture". Cell Transplantation. 2001, Vol. 10, pages 441-445.).

Claims as above.

The reference by Furukawa et al. discloses a tissue-like organization of cells that are three-dimensional fibroblast aggregates obtained by growing cells in suspension of high initial seeding density in a culture vessel with 35 mm diameter. Thus, the cited preparation of cells is free of scaffold/matrix requirements within the meaning of the claims and the cited preparation of cells as a whole within the culture vessel has the diameter "at least 3 mm" and more. The reference describes that cell preparation is made by inoculating 5 ml suspension with $1.66x10^6$ cells/ml into a dish having diameter 35 mm and, thus the seeding density is as follows: 5 x $1.66x10^6/5.4\ cm^2 = 1.5x10^6\ cells/cm^2$, wherein $\pi r^2 = 3.14x(3.5cm/2)^2 = 5.4\ cm^2$. The presently claimed invention encompasses the use of initial seeding density of $3x10^5\ cells/cm^2$ of a culture vessel. Thus, the initial seeding density of the cited cell preparation falls within the claimed range.

Although the cited reference describes that fibroblast cells are grown with shaking or by rotating culture, the final product is 3-dimentional tissue-like organizations of cells as the claimed product. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. MPEP 2113. Although the cited reference describes that fibroblast cells are grown on medium with supplements including insulin, dexamethasone, etc. the claimed invention does not exclude the supplements described in the

cited reference. Moreover, the final components of the claimed product are not defined by the claimed invention.

The cited reference also teaches that aggregates of dermal fibroblasts have been combined with polymer materials (figure 5; page 444, col. 2, last par.) within the meaning of the claims 33 and 34.

Thus, the 3-dimentional tissue-like dermal fibroblast aggregates as a whole mass without matrix or combined with polymer materials disclosed by Furukawa et al. are identical to the claimed tissue-like organization of cells made from dermal fibroblasts.

Therefore, the cited document anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 24-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,755,814 (Berg et al.) and Furukawa et al. ("Formation of human fibroblast aggregates (spheroids) by rotational culture". Cell Transplantation. 2001, Vol. 10, pages 441-445.).

Claims are directed to a 3-dimensional cell mass or a 3-dimensional tissue-like preparation of cells with a diameter of at least 3 mm and more wherein the cells have been grown in the absence of matrix. The cells are dermal fibroblasts. Some claims are further drawn to the use of cells that have been grown a basic serum supplemented medium, at initial cell density of

$3x10^5$ cells/cm^2 and in a regular or simple culture vessel. Some claims are further drawn to a combination of cell preparation and matrix.

US 5,755,814 (Berg et al.) discloses a preparation of dermal fibroblasts grown in a culture vessel in a basic DMEM supplemented with serum, in the absence matrices (col. 9, lines 38-46) at seeding density of 4.8×10^5 cells/cm^2 as explained above. The final matrix-free cell preparation has been grown in a well with a diameter more than 3 mm. The cited patent is lacking particular disclosure about a combination of a matrix and a cell preparation that is initially obtained in the absence of matrix.

However, the reference by Furukawa et al. teaches inoculation of dermal fibroblast aggregates that are initially grown in the absence of matrix into/onto the sheets of biodegradable polymer materials (page 444, col. 2, last par.).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to combine matrix materials with the cell mass grown at high density in the absence of matrix with a reasonable expectation of success in obtaining tissue-engineered dermal grafts suitable for wound healing as taught and/or by Furukawa et al. (page 445, col.1, line 1). One of skill in the art would have been motivated to modify diameter of cell preparations depending on dimension of implantation site of the cell graft, for example.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicant's arguments filed 7/17/2006 have been fully considered but they are not persuasive.

With regard to the cited patent US 5,755,814 (Berg et al.) applicants argue that the claimed cell preparations are distinct because they are made without the aid of a matrix (page 10). However, US 5,755,814 discloses cell preparations that are obtained both with matrix and without matrix. Applicants appear to argue that the US' 814 cell preparation made without matrix is not the main embodiment of the cited patent. However, the patent disclosure is relied upon for all it contains. Applicants also argue that the cell preparations disclosed by US 5,755,814 is made by using a different cell density and a different dish diameter. Upon review of the reference it is not found true, for example: see calculations as explained above. A culture plate well has 0.9 cm diameter not 1.5 cm as argued (page 9).

With regard to the cited reference by Furukawa et al. applicants argue that the cited cell preparations are small aggregates and that they are not sheet-like in nature (page 12). Yet, the aggregates as a whole mass collected from the 35 mm dish is reasonably expected to has a diameter at least 3 mm within the meaning of claim 24. Further, the cited reference also teaches that aggregates of dermal fibroblasts have been combined with sheet-like polymer materials (figure 5; page 444, col. 2, last par.) within the meaning of the claims 33 and 34. Thus, even if the aggregates might not have a sheet-like configuration "immediately upon formation" (claim 35), the sheet like configuration is further provided upon combination with polymers.

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

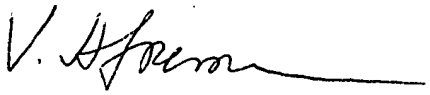
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova
AU 1651
September 26, 2006



VERA AFREMOVA
PRIMARY EXAMINER